

CLAIMS:

1. An isolated nucleic acid molecule encoding a polypeptide comprising all or a portion of a human, rat or murine KCNQ5 protein.
2. An isolated polynucleotide having a nucleic acid sequence which is capable of hybridizing under at least medium stringency conditions with the polynucleotide sequence presented as SEQ ID NO: 1, its complementary strand, or a subsequence thereof.
3. The isolated polynucleotide according to claim 2, being at least 65% homologous, preferably more than 70%, more preferred more than 80%, even more preferred more than 90%, most preferred more than 95%, homologous to the polynucleotide sequence presented as SEQ ID NO: 1.
4. The isolated polynucleotide according to any of claims 1-3, wherein said polynucleotide is a cloned polynucleotide.
5. The isolated polynucleotide according to claim 4, wherein the polynucleotide is cloned from, or produced on the basis of a cDNA library.
6. The isolated polynucleotide according to claim 1, comprising the polynucleotide sequence presented as SEQ ID NO: 1.

7. The isolated polynucleotide according to claim 1, encoding a potassium channel, or a potassium channel subunit.
8. The isolated polynucleotide according to claim 7, encoding the KCNQ5 potassium channel subunit comprising the amino acid sequence represented by SEQ ID NO: 2.
9. The isolated polynucleotide according to claim 7, encoding a KCNQ5 variant, which variant has an amino acid sequence that has been changed by deletion of an amino acid residue, by insertion of an additional amino acid residue, or by substitution of an amino acid residue at one or more positions.
10. The isolated polynucleotide according to claim 9, wherein said variant has an amino acid sequence that has been changed at one or more positions located in the conserved regions, as defined by Table 1.
11. The isolated polynucleotide according to claim 9, wherein said variant is G329S (KCNQ1 numbering), or KCNQ5/G278S.
12. A vector construct comprising the polynucleotide according to claim 11.

13. A recombinantly produced polypeptide encoded by the polynucleotide according to claim 1.

14. The polypeptide according to claim 13, wherein said polypeptide is a KCNQ5 potassium channel subunit having the amino acid sequence presented as SEQ ID No. 2.

15. The polypeptide of either of claims 13-14, comprising a molecular weight of approximately 99 kDa.

16. The polypeptide of claim 13, comprising six transmembrane domains, a P-loop, and a carboxy-terminal conserved cytoplasmic region (the "A-domain").

17. The polypeptide according to claim 13, wherein said polypeptide is a KCNQ5 variant, which variant has an amino acid sequence that has been changed by deletion of an amino acid residue, by insertion of an additional amino acid residue, or by substitution of an amino acid residue at one or more positions.

18. The polypeptide according to claim 17, wherein said variant has an amino acid sequence that has been changed at one or more positions located in the conserved regions, as defined by Table 1.

19. The polypeptide according to claim 18, wherein said variant is G329S (KCNQ1 numbering), or KCNQ5/G278S.
20. A cell genetically manipulated by the incorporation of a heterologous polynucleotide according to claim 1 or a vector construct according to claim 12.
21. The cell according to claim 20, genetically manipulated by the incorporation of a KCNQ5 channel subunit having the amino acid sequence presented as SEQ ID NO: 2.
22. The cell according to claim 20, genetically manipulated by the incorporation of a KCNQ5 variant, wherein said variant has an amino acid sequence that has been changed by deletion of an amino acid residue, by insertion of an additional amino acid residue, or by substitution of an amino acid residue at one or more positions.
23. The cell according to claim 22, wherein said variant has an amino acid sequence that has been changed at one or more positions located in the conserved regions, as defined by Table 1.
24. The cell according to claim 20, genetically manipulated to co-express one or more KCNQ channel subunits.
25. The cell according to claim 24, genetically manipulated to co-express KCNQ5 and KCNQ1 channel subunits;

KCNQ5 and KCNQ2 channel subunits;
KCNQ5 and KCNQ3 channel subunits;
KCNQ5 and KCNQ4 channel subunits;
KCNQ5 and KCNQ1 and KCNQ2 channel subunits;
KCNQ5 and KCNQ1 and KCNQ3 channel subunits;
KCNQ5 and KCNQ1 and KCNQ4 channel subunits;
KCNQ5 and KCNQ2 and KCNQ3 channel subunits;
KCNQ5 and KCNQ2 and KCNQ4 channel subunits;
KCNQ5 and KCNQ3 and KCNQ4 channel subunits;
KCNQ5 and KCNQ1 and KCNQ2 and KCNQ3 channel subunits;
KCNQ5 and KCNQ1 and KCNQ2 and KCNQ4 channel subunits;
KCNQ5 and KCNQ1 and KCNQ3 and KCNQ4 channel subunits; or
KCNQ5 and KCNQ2 and KCNQ3 and KCNQ4 channel subunits.

26. The cell according to claim 24, genetically manipulated to co-express KCNQ2 or KCNQ3, and KCNQ5 channel subunits.

27. The cell according to claim 20, wherein said cell is an eukaryotic cell, in particular a mammalian cell, an oocyte, or a yeast cell.

28. The cell according to any claim 27, being a human embryonic kidney (HEK) cell, a HEK 293 cell, a BHK21 cell, a Chinese hamster ovary (CHO) cell, a *Xenopus laevis*

oocyte (XLO) cell, a COS cell, or any other cell line able to express KCNQ potassium channels.

29. A membrane preparation derived from a cell according to claim 20.

30. A method for obtaining a substantially homogeneous source of a human potassium channel, comprising a KCNQ5 subunit, which method comprises the steps of culturing a cellular host having incorporated expressibly therein a polynucleotide according to claim 1, or a vector construct according to claim 12, and then recovering the cultured cells.

31. The method of claim 29, further comprising the subsequent step of obtaining a membrane preparation from the cultured cells.

32. A method of screening a chemical compound for capability of binding to a potassium channel comprising at least one KCNQ5 channel subunit, which method comprises the steps of

- (i) subjecting a KCNQ5 channel subunit containing cell, or a membrane preparation hereof, to the action of a KCNQ5 binding agent to form a complex with the KCNQ5 channel subunit containing cell;
- (ii) subjecting the complex of step (i) to the action of the chemical compound to be tested; and

(iii) detecting the displacement of the KCNQ5 binding agent from the complex with the KCNQ5 channel subunit containing cell.

33. The method of claim 32, wherein the KCNQ5 channel subunit containing cell is a cell according to claim 20, or a membrane preparation according to claim 29.

34. The method of claim 32, wherein the KCNQ5 binding agent is

- (i) radioactively labeled 1,3-dihydro-1-phenyl-3,3-bis-(4-pyridylmethyl)-2H-indol-2-one (Linopirdine); or
- (ii) radioactively labeled 10,10-bis-(4-pyridinyl-methyl)-9-(1 OH)-anthra-cenone (XE991).

35. The method of claim 34, wherein said compounds have been marked with ^3H .

36. The method of either of claims 32-33, wherein the displacement of the KCNQ5 binding agent from the complex with the KCNQ5 channel subunit containing cell is detected by measuring the amount of radioactivity by conventional liquid scintillation counting.

37. A method of screening a chemical compound for activity on a potassium channel comprising at least one KCNQ5 channel subunit, which method comprises the steps of

- (i) subjecting a KCNQ5 channel subunit containing cell, or a membrane preparation hereof, to the action of the chemical compound; and

(ii) monitoring the membrane potential, the current, the potassium flux, or the secondary calcium influx of the KCNQ5 channel subunit containing cell.

38. The method of claim 37, wherein the KCNQ5 channel subunit containing cell is a cell according to claim 20, or a membrane preparation according to claim 29.

39. The method of claim 37, wherein monitoring of the membrane potential of the KCNQ5 channel subunit containing cell is performed by patch clamp techniques.

40. The method of claim 37, wherein monitoring of the membrane potential of the KCNQ5 channel subunit containing cell is performed using fluorescence methods.

41. A chemical compound identified by the method of claim 32 and/or claim 37.

42. A method for diagnosis, treatment, prevention or alleviation of diseases related to diseases or adverse conditions of the CNS, including affective disorders, Alzheimer's disease, anxiety, ataxia, CNS damage caused by trauma, stroke or neurodegenerative illness, cognitive . deficits, compulsive behavior, dementia, depression, Huntington's disease, mania, memory impairment, memory disorders, memory dysfunction, motion , disorders, motor disorders, neurodegenerative diseases, Parkinson's disease and Parkinson-like motor disorders, phobias, Pick's disease, psychosis, schizophrenia, spinal cord damage, stroke, tremor, seizures, convulsions and epilepsy, comprising the step of administering the chemical compound of claim 41 to a subject in need thereof.

43. The method according to claim 42, wherein the chemical compound is 1,3-dihydro-1-phenyl-3,3-bis-(4-pyridylmethyl)-2H-indol-2-one (Linopirdine); or 10,10-bis-(4-pyridinyl-methyl)-9-(1 OH)-antracenone (XE991).

44. A method for determining individuals having mutations in the polynucleotide sequence according to claim 1, comprising the step of screening of genetic materials collected from mammalian tissues, in particular human tissues with the polynucleotide sequence according to claim 1, or a vector construct according to claim 12.

45. A transgenic animal comprising a knock-out mutation of the endogenous *KCNQ5* gene, a mutated *KCNQ5* gene, or genetically manipulated in order to over-express the *KCNQ5* gene or to over-express mutated *KCNQ5* gene.

46. The transgenic animal according to claim 45, wherein said animal is a knock-out animal in which the gene is totally deleted in a homozygous state.

47. The transgenic animal according to claim 45, comprising a mutated *KCNQ5* gene.

48. The transgenic animal according to claim 45, wherein said animal is a transgenic rodent, in particular a hamster, a guinea pig, a rabbit, or a rat, a transgenic pig, a transgenic cattle, a transgenic sheep, or a transgenic goat.

49. A method for *in vivo* screening of therapeutic compounds, comprising the step of administering said compounds to the transgenic animal according to claim 45.

50. The method according to claim 49, for the screening of drugs affecting diseases or conditions associated with malfunction of the CNS, such as affective disorders, Alzheimer's disease, anxiety, ataxia, CNS damage caused by trauma, stroke or neurodegenerative illness, cognitive deficits, compulsive behavior, dementia, depression, Huntington's disease, mania, memory impairment, memory disorders, memory dysfunction, motion disorders, motor disorders, neurodegenerative diseases, Parkinson's disease and Parkinson-like motor disorders, phobias, Pick's disease, psychosis, schizophrenia, spinal cord damage, stroke, tremor, seizures, convulsions and epilepsy.

51. An antibody capable of binding one or more polypeptides as claimed in claim 13.

52. The antibody of claim 51, wherein said antibody is a monoclonal antibody.